

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION See paragraph 2 below

International application No.
PCT/US2004/002543

International filing date (day/month/year)
30.01.2004

Priority date (day/month/year)
30.01.2003

International Patent Classification (IPC) or both national classification and IPC
C07G17/00, C07H19/00, C07H19/16

Applicant
UNIVERSITY OF MARYLAND, BALTIMORE

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 a sequence listing
 table(s) related to the sequence listing
 - b. format of material:
 in written format
 in computer readable form
 - c. time of filing/furnishing:
 contained in the international application as filed.
 filed together with the international application in computer readable form.
 furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. The following document has not been furnished:

- copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).
- translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

the entire international application,
 claims Nos. 1-10,12-23

because:

the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):
 the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-10,12-23 are so unclear that no meaningful opinion could be formed (specify):

see separate sheet

the claims, or said claims Nos. 1-10,12-23 are so inadequately supported by the description that no meaningful opinion could be formed.
 no international search report has been established for the whole application or for said claims Nos. 1-10,12-23
 the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	<input type="checkbox"/> has not been furnished <input type="checkbox"/> does not comply with the standard
the computer readable form	<input type="checkbox"/> has not been furnished <input type="checkbox"/> does not comply with the standard

the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
 See separate sheet for further details

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	11
	No: Claims	
Inventive step (IS)	Yes: Claims	11
	No: Claims	
Industrial applicability (IA)	Yes: Claims	11
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Present claims 1-10, 12-23 relate to a compounds defined by reference to a desirable characteristic or property, namely compounds "that bind to the hemoglobin binding site on cytochrome b5 and competitively inhibits hemoglobin binding to cytochrome b5" The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds having the following simultaneous characteristics :

Compounds wherein :

- 1) R1 is defined as in claims 2-4 (a linear or cyclic polyamine or hexacyclene) and
- 2) R2 is a moiety that links R1 and R3 (whatever this moiety may represent) and
- 2) R3 is defined as in claims 7-9 (ATP or ATP analogues).

The reason why no opinion will be given concerning claim 1-10, 12-23 is that R1 and R3 are essential technical features for the present invention and therefore, not only need to be clearly defined (and can be clearly defined, that is in concrete terms and not by functional definitions), but also need to be **simultaneously** present to define the scope and protection of the present invention. As it is not the case for claims 1-10, 12-23, these claims are considered unclear (Art. 6 PCT).

Would be considered allowable and clear, claims wherein R1 and R3 are specified as above. R2 does not need to be defined more precisely to fulfill the requirements of clarity as R2 does not represent the core of the invention.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The subject-matter of claim 11 concerns compounds consisting in a R1-R2-R3 wherein R1 is hexacyclene, R3 β -nicotine amide dinucleotide and R2 a moiety that binds R1 and R3. These compounds are useful for the treatment of sickle cell disease by binding to the hemoglobin binding site on cytochrome b5 and competitively inhibits hemoglobin binding to cytochrome b5.

Since none of the cited prior art suggest or disclose such compounds, the subject-matter of claim 11 is considered new and inventive according to Art. 33(2) and (3) PCT.

The subject-matter of claim 11 also complies with the requirement of Art 33(4) PCT.

Re Item VIII

Certain observations on the international application

- 1) When drafting a new set of claims, the applicant is advised to take into consideration the cited documents which could eventually be relevant to the issue of novelty.
- 2) For the assessment of the present claims 20,21-23 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Claim 22 is however considered as industrially applicable as the method claimed is performed *ex vivo*.